IN THE SPECIFICATION:

Please amend the paragraph beginning at page 5, line 28, as follows:

MF 12/23/02 FIG. 10 A, B, C, D shows an alignment of the amino acid sequence of human β-secretase ("Human Imapain.seq,") (SEQ ID NO: 2) compared to various mouse constructs (SEQ ID NOS:65 and 105-108).

Please amend the paragraph at page 6, lines 18 as follows:

FIG. 19 shows a schematic of an APP substrate fragment (SEQ ID NOS:103 and104), and it's use in conjunction with antibodies SW192 and 8E-192 in the assay.

Please amend the paragraph at page 6, lines 20 as follows:

FIG. 20 shows a schematic of an APP substrate fragment (SEQ ID NOS:103 and104), and it's use in conjunction with antibodies SW192 and 8E-192 in the assay.

Please add the following paragraphs at page 8, lines 13, after the paragraphs added previously in the preliminary amendment mailed July 28, 2000.

SEQ ID NO:103 is the β-secretase cleavage sites in the wild-type APP sequence.

SEQ ID NO:104 is the β-secretase cleavage sites in the Swedish APP sequence.

SEQ ID NOS:105-109 are mouse constructs in alignment to the human β-secretase containing portions of β-secretase of Figure 10.

Please delete the paragraph at page 8, line 11, and replace it with the following replacement paragraph.

SEQ ID NO: 73 is P4-P4'staD→V.

Please amend the paragraph beginning at page 24, line 8, as follows:

The full-length open reading frame (ORF) of human β-secretase is described above, and its sequence is shown in FIG. 2A as SEQ ID NO: 2. However, as mentioned above, a further discovery of the present invention indicates that the predominant form of the active, naturally occurring molecule is truncated at the N-terminus by about 45 amino acids. That is, the protein purified from natural sources was N-terminal sequenced according to methods known in the art

(Argo Bioanalytica, Morris Plains, NJ). The N-terminus yielded the following sequence: ETDEEPEEPGRRGSFVEMVDNLRG... (SEQ ID NO: 55). This corresponds to amino acids 46--69 of the ORF-derived putative sequence. Based on this observation and others described below, the N-terminus of an active, naturally occurring, predominant human brain form of the enzyme is amino acid 46, with respect to SEQ ID NO: 2. Further processing of the purified protein provided the sequence of an internal peptide: IGFAVSACHVHDEFR (SEQ ID NO: 56), which is amino terminal to the putative transmembrane domain, as defined by the ORF. These peptides were used to validate and provide reading frame information for the isolated clones described elsewhere in this application.

REMARKS

Applicants request entry of this amendment in adherence with 37 C.F.R. §§1.821 to 1.825. This amendment is accompanied by a floppy disk containing SEQ ID NOS: 1-108, in computer readable form, and a paper copy of the sequence information which has been printed from the floppy disk. The information contained in the computer readable disk of was prepared through the use of the software program "PatentIn 2.1" and is identical to that of the paper copy. This amendment contains no new matter.

The corrections and additions to the specification requested herein are corrections needed to conform the specification to the Sequence Listing, as explained below.

In The BRIEF DESCRIPTION OF THE DRAWINGS section sequence identifiers SEQ ID NO: 103 and 104, and SEQ ID NO:105-108 were added to the description of Figures 19B and 10 respectively in order to comply with the requirements 37 C.F.R. §1.821.

The paragraph containing descriptor of SEQ ID NO: 73 was replaced with a replacement paragraph to remove the recited sequence, which correctly describes SEQ ID NO: 72 (obvious from the length of the sequence), but which is superfluous in view of the Sequence Listing.

A new paragraph for each of the descriptors of SEQ ID NOS: 103-108 was added after the new paragraph containing descriptor of SEQ ID NO:102, in view of their addition to the sequence listing, as described with reference to Figure 19B and Figure 10.

Amendments to the paragraph beginning on page 24, line 8, merely clarify the nature of molecule described. Support for these amendments can be found on page 7, lines 5-8, of the application as filed.